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10/582,002	06/07/2006	Manabu Watanabe	Q95278	8934

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	PAPER NUMBER
1652	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,002	WATANABE ET AL.	
	Examiner	Art Unit	
	IQBAL H. CHOWDHURY	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-4, 8-15 and 17-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7,16,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/06, 09/07, 03/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/JP04/18184.

Claims 1-20 are currently pending.

The preliminary amendment filed on April 23, 2009, amending claim 1 is acknowledged.

Election/Restriction

Applicant's election without traverse of Group II claim(s) 5-7, 16 and 19-20, drawn to a protein or modified protein in which one or plural amino acids are deleted, substituted, inserted or added in the amino acid sequence of SEQ ID NOs: 2, 4, 38 or 40 having endoglucanase activity, wherein N-terminal amino acid is pyroglutamic acid in the communication filed on April 23, 2009 is acknowledged. Claims 1-4, 8-15 and 17-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicants' arguments regarding rejoinder issue is noted. Applicants have the right to rejoin invention directed to a method of using a product, when the product claims are allowed provided that applicants amend the methods claims to conform to the same scope as that of the allowed product claims.

Claims 5-7, 16 and 19-20 are present for examination.

Priority

Acknowledgement is made of applicants claim for international application of PCT/JP04/18184 filed on 12/7/2004 and foreign priority under 35 U.S.C. 119(a)-(d) to a

foreign patent application JAPAN 2003-409692 filed on 12/8/2003 without English translation.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 6/47/2006, 9/24/2007 and 3/5/2009 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is considered by the examiner. The signed copies of IDS are enclosed herewith.

Drawings

Drawings submitted on 6/7/2006 are accepted by the Examiner.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 14). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 16, 19 and 20 are objected to as depending from non-elected claims. Appropriate correction is requested.

Claim 7 is objected to in the recitation "SEQ ID NO: 2, 4, 38 or 40, and having endoglucanase activity, whose reduction in the presence of the surfactant is small", which should be "SEQ ID NO: 2, 4, 38 or 40, and having endoglucanase activity,

wherein the endoglucanase activity reduction in the presence of surfactant is small".

Appropriate correction is requested.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained. Claim 6 is indefinite in the recitation "suppressing a reduction in an endoglucanase activity", wherein the phrase "suppressing a reduction" is a relative term, which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The claim should define and clearly state as to what the reduction of endoglucanase activity in presence of surfactant is being compared, i.e. suppressing a reduction --- compared to what?

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 7 is indefinite in the recitation "endoglucanase activity whose reduction in the presence of surfactant is small", wherein the phrase "small" is relative term, which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and

one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The claim should define and clearly state as to what the "reduction ---- is small" of said polypeptide activity is being compared.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7, 16 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5-7, 16 and 19-20 are directed to any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at

least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical*).

Thus, claims are drawn to any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity. Claims are drawn to any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, i.e. the phrase "one or more" interprets as any number of mutations of SEQ ID NOs: 2, 4, 38 or 40 as polypeptides having no structural feature. No information, beyond the characterization of protein having endoglucanase activity has been provided, which would indicate that they had possession of the claimed genus. The specification does not contain any disclosure of the structures of the all the mutants and variants of any modified protein from any source or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity (part B)

within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including mutants, variants and peptides which can have wide variety structures. Therefore, many structurally unrelated polypeptides are encompassed within the scope of the claim. The specification discloses the structure of only a 4 representative species of the claimed genus, i.e. SEQ ID NO: 2, 4, 38 or 40, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 5-7, 16 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modified cellulase enzymes of SEQ ID NOs: 2, 4, 38 or 40 having endoglucanase activity, wherein the reduction of endoglucanase activity in presence of surfactant is small compared to in absence of surfactant, does not reasonably provide enablement for any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity (part B); or any homologous protein having at least 85% homology to SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity, wherein the reduction of endoglucanase activity in presence of surfactant is small. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731,737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows:

(1) quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence and absence of working examples, (4) the nature of the invention, (5) the state of prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The factors, which have, lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed below:

The breadth of the claims:

Claim 7 encompasses any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity (part B) or any homologous protein having at least 85% homology, i.e. 15% non-homologous proteins of SEQ ID NO: 2, 4, 38, or 40 having an endoglucanase activity, wherein the reduction of endoglucanase activity in presence of surfactant is small. The scope of the claims is not commensurate with the enablement provided by the

disclosure with regard to the large number of proteins including mutants, variants and recombinants encompassed by the claims. In the instant case the disclosure is limited to the nucleotide and encoded amino acid sequence of only four proteins of SEQ ID NOs: 2, 4, 38 or 40.

The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art:

The amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In the instant case, any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity or any homologous protein having at least 85% homology, i.e. 15% non-homologous proteins of SEQ ID NO: 2, 4, 38, or 40 comprise many mutants, variants and recombinants. The art clearly teaches the high level of unpredictability with regard to the effect of structural changes in a protein's activity when no guidance/knowledge as to which amino acids are required for activity has been provided. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple

modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. For example, Branden et al. (1991 teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing de novo stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. (1999), where it is shown that even small amino acid changes result in enzymatic activity changes.

The amount of direction or guidance presented and the existence of working examples:

The specification discloses cellulase enzymes of SEQ ID NOs: 2, 4, 38 or 40, wherein the reduction of endoglucanase activity in presence of surfactant is small, However, the specification fails to provide any clue as to the structural elements required in , any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity or any homologous protein having at least 85% homology, i.e. 15% non-homologous proteins of SEQ ID NO: 2, 4, 38, or

40 known in the art that are essential for any protein to display endoglucanase enzymatic activity. No correlation between structure and function has been presented.

The specification does not support the broad scope of the claims which encompass, any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity or any homologous protein having at least 85% homology, i.e. 15% non-homologous proteins of SEQ ID NO: 2, 4, 38, or 40 because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting endoglucanase activity and; (B) the general tolerance of polypeptides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any polypeptide amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The quantity of experimentation required practicing the claimed invention based on the teachings of the specification:

While methods of generating or isolating variants of a polynucleotide were well known in the art at the time of invention, it is not routine in the art to screen by trial and error process for (1) , any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid

sequence of SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity or any homologous protein having at least 85% homology, i.e. 15% non-homologous proteins of SEQ ID NO: 2, 4, 38, or 40; and (2) an essentially infinite number of mutations of any protein sequence, which is 85% homologous to SEQ ID NO: 2, 4, 38, or 40. The amino acids modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any modified protein from any source having endoglucanase activity or any modified protein comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, and having an endoglucanase activity or any homologous protein having at least 85% homology, i.e. 15% non-homologous proteins of SEQ ID NO: 2, 4, 38, or 40. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any modified protein comprising endoglucanase activity having the desired biological characteristics

is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-6, 7, 16, 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Kleywegt et al. (The crystal structure of the catalytic core domain of endoglucanase I from Trichoderma reesei at 3.6 A resolution, and a comparison with related enzymes. Mol Biol. 1997 Sep 26;272(3):383-97, see IDS). Kleywegt et al. teach catalytic core domain of an endoglucanase I (EG I), a modified from of EG I, wherein catalytic core domain comprises amino acid residue 1-374, wherein amino acid at position 1 of N-terminus is glutamine and a crystal structure. Kleywegt et al. also teach alignment of the amino acid sequences of the catalytic core domains of EG I and CBH I, wherein N-terminal amino acid is glutamine, which will be instantly converted or cyclized to pyroglutamic acid in solution (Abstract, Fig. 4). Kleywegt et al. further teach recombinant expression of said modified protein in Trichoderma reesei (page 393, left column, and paragraph 2). Claim 6 is included in this rejection because the modified protein of claim 6 is structurally the same as the modified protein of claim 5, which is structurally the same as the protein taught by Kleywegt et al., with the exception that the

modified protein of claim 6 is obtainable by the method referred to in claim 6. As the referred to method does not appear to structurally alter the modified protein of claim 5, the protein of claim 6, is included in this rejection.Thus, Kleywegt et al. teach a modified protein having endoglucanase activity, and the protein of the Kleywegt et al. meets the claim limitation of claim 6. Claim 7 is included in this rejection because of the limitation in part (b), which interprets any protein having endoglucanase activity due to the recitation of one or plural amino acids are deleted, substituted, inserted, or added in the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40, which renders the protein having no structure and the protein of Kleywegt et al. meets the claim limitation structurally and functionally having same endoglucanase activity. Thus, the protein of Kleywegt et al. meets the claim limitation.

Furthermore, because the modified protein having endoglucanase activity of the claimed enzyme (as written) and that of modified enzyme of the reference is one and the same as evidenced by Kleywegt et al., Examiner takes the position that the modified protein having endoglucanase activity disclosed in the Kleywegt et al. reference inherently have the property of suppressing the reduction (if any) in endoglucanase activity in the presence of the surfactant due to modification of the enzyme or "endoglucanase activity reduction in the presence of surfactant is small". Since the Office does not have the facilities for examining and comparing applicants' modified enzyme with the modified enzyme of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the

prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Therefore, Kleywegt et al. anticipates claims 5-6, 7, 16, 19 and 20 of the instant application as written.

Conclusion

Status of the claims:

Claims 1-20 are pending.

Claims 1-4, 8-15 and 17-18 are withdrawn.

Claims 5-7, 16 and 19-20 are rejected.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Iqbal Chowdhury, Patent Examiner
Art Unit 1652

/Richard G Hutson/
Primary Examiner, Art Unit 1652